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Methoxycarbonylation of Styrene Using a New Type of Palladium Complexes Bearing *P,N*-donor Ligands as Catalysts

Gabriel Abarca · Kareen Brown · Sergio A. Moya · J. Carles Bayón · Pedro A. Aguirre

Abstract Palladium complexes of the type [Pd(L)Cl(PPh$_3$)]Cl (L = 2-diphenylphosphinoamino)pyrimidine, or 2-diphenylphosphinoaniline), generated in situ by addition of one equivalent of PPh$_3$ to the corresponding neutral complexes [Pd(L)Cl$_2$], were tested as catalysts for the methoxycarbonylation of styrene. The catalyst containing the pyrimidinyl ligand shows almost complete chemo- and regioselectivity together with a high conversion rate. However, in identical conditions, the [Pd(Ph$_2$PNHC$_6$H$_4$PPh$_2$)Cl$_2$] complex, where the *P,N*-ligand has been replaced by a related bidentate *P*-donor one, shows a significantly lesser performance.

Graphical Abstract
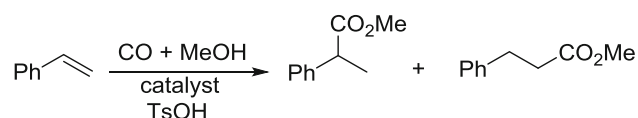
1 Introduction

Among bidentate ligands, diphosphines have played a preponderant role in the area of transition metal catalyzed reactions. However, heterobidentate *P,N*-donor ligands have emerged lately as an important class of ligands that have been applied in various catalytic transformations, such as hydrogenation of alkenes [1, 2], hydrogen transfer reactions [3], Suzuki–Miyura couplings [4, 5], arylation of unactivated arenes [6], alkylation of anilines by alcohols [7] and allylic substitution [8, 9], among others. Nevertheless, this type of ligands has been scarcely used in metal catalyzed carbonylation reactions, and almost in all reported cases Pd was the metal used. For instance, Pd complexes with *P,N*-donor ligands are active in the reductive carbonylation of nitroaromatics [10] and CO–alkene polymerization [11, 12], but the most important process of this type is undoubtedly the industrial carbonylation of alkynes to produce methyl methacrylate and related products catalyzed by a palladium complex of 2-diphenylphosphino-pyridine (Ph$_2$Ppy), Fig. 1 [13]. Furthermore, a Pd(II) complex of 2-(diphenylphosphinoamino)-pyridine (Ph$_2$PNHpy) is active in the carbonylation of ethanol to ethyl propionate [14].
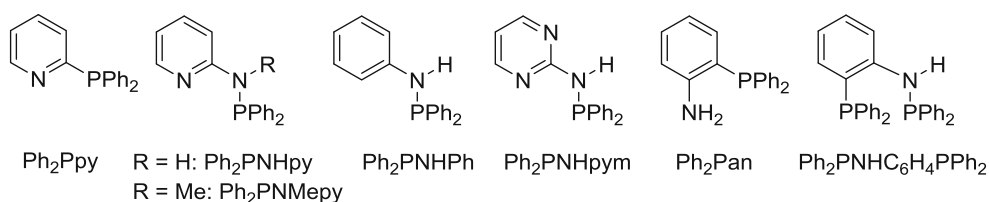
The alcoxycarbonylation of olefins belongs to the family of relevant carbonylation reactions that are efficiently catalyzed by homogenous palladium complexes [15–18]. The methoxycarbonylation of ethylene is used for the industrial production of methyl propanoate [19]. Moreover, a series of commercial non-steroidal anti-inflammatory agents are accessible through the reaction of vinyl aromatics with CO

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Fig. 1 Phosphorus–nitrogen ligands used in methoxycarbonylation reaction of olefins

and H_2O or alcohols in the presence of a Pd catalyst [20]. Although two mechanisms have been proposed for this reaction, recent evidences favor the one that involves a Pd(II)-H species, which reacts with the alkene, followed by a CO insertion in the Pd-alkyl fragment, and ending with a nucleophilic attack of the alcohol to the acyl intermediate [21].

Only two previous reports deal with a methoxycarbonylation reaction catalyzed by Pd(II)-*P*,*N*-donor ligands. A palladium catalyst bearing a chiral ferrocenyl ligand with diphenylphosphino and dimethylamino fragments was essayed by Kollár et al. in the methoxycarbonylation of styrene [22]. More recently, we reported that the complex [PdCl(PPh₃)(Ph₂PNHpy)]Cl is a remarkably active and selective catalyst for the methoxycarbonylation of styrene. This catalyst is also moderately active with 1-hexene and even with cyclohexene, but rates achieved with these substrates are lower than with styrene. In identical conditions, other closely related ligands, such as 2-(diphenylphosphinoaminomethyl)pyridine (Ph₂PNMepy) or (diphenylphosphino)phenylamine (Ph₂PNHPh) (Fig. 1), perform significantly worse, suggesting that both the pyridine and the NH fragments are crucial in the performance of Ph₂PNHpy as ligand for the methoxycarbonylation of vinylarenes [23]. However, the role of these two fragments in the catalytic mechanism was not completely understood.

A recent report revealed that the complex [Pt(^{t}Bu₂PNHpy)Me₂] undergoes partial rollover cyclometalation of the pyridyl ring concurrent with methane evolution (scheme 1) [24]. Because of the similarity of this ligand to Ph₂PNHpy, it is not possible to exclude a priori that a metalation process also takes place during the methoxycarbonylation reaction. The formation of this cyclometalated product
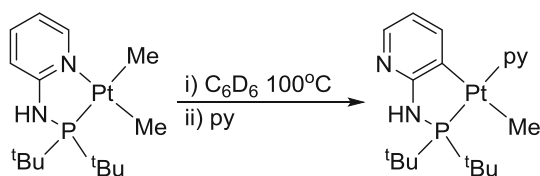
could be the responsible for the unusual behavior of Ph₂-PNHpy in this catalytic reaction. Notice the similarity of the product of the reaction in Scheme 1 with the Pd-alkyl intermediate in the methoxycarbonylation process.

Therefore, in order to get some insight about the role of the pyridyl and the NH fragments of the ligands in the Pd catalyzed methoxycarbonylation of alkenes, we have undertaken a study of this reaction by using two *P*,*N*-donor ligands. On the one hand, the 2-(diphenylphosphinoamino)pyrimidine ligand (Ph₂PNHpym) (Fig. 1) was selected because of the similarity with the pyridine Ph₂-PNHpy, and because its Pd complex cannot undergo the cyclometalation described above. On the other hand, the 2-(diphenylphosphino)aniline ligand (Ph₂Pan) was selected as an example of a ligand with a more basic *N*-donor atom, preserving a NH fragment. Furthermore, a bidentate *P*-donor ligand, *N*,2-bis(diphenylphosphino)benzeneamine (Ph₂PNHC₆H₄PPh₂), again containing the same NHPPh₂ fragment than Ph₂PNHpy (see Fig. 1), was also investigated in this reaction to clarify if the beneficial effect of the NH fragment in the reaction performance is exclusive of the heterobidentate *P*,*N*-donor ligands, or if it applies to other ligands lacking the hemilabile capacity.

2 Experimental Section

2.1 General

All manipulations were carried out under nitrogen using standard Schlenk techniques. Organic solvents and styrene were purified by distillation over standard agents and deoxygenated prior to use. 2-(diphenylphosphino)aniline (Ph₂Pan) was synthesized by a reported procedure [25]. Commercial products were used without further purification. NMR data were obtained on Bruker 300 or 400 MHz spectrometers, and spectra were referenced with TMS as internal standard (^{1}H) or with 85 % H_3PO_4 as external standard (^{31}P). GC analysis was performed on a Hewlett-Packard Agilent 5890 N chromatograph with a flame ionization detector and equipped with an HP-5 column.

Scheme 1 Cyclometalation of the platinum complex with a phosphorus–nitrogen ligand

2.2 Synthesis of Ligands

2.2.1 2-(Diphenylphosphinoamino)pyrimidine (Ph$_2$PNHpym)

A very short crystallographic communication on this ligand, without synthetic or other characterization details, was previously reported [26]. Therefore, a complete description of the synthesis and spectroscopic data for Ph$_2$PNHpym is described here. A mixture of 2-aminopyrimidine (500 mg, 5.25 mmol) and triethylamine (0.74 mL, 5.25 mmol) was dissolved in THF (15 mL). The solution was cooled at 0 °C and Ph$_2$PCl (1.0 mL, 5.25 mmol) was slowly added. The reaction was allowed to reach room temperature and stirred further for 6 h. After this time, the ammonium salt was separated by filtration and the solvent was removed under vacuum. The oily residue obtained was dissolved in CHCl$_3$ and precipitated with Et$_2$O (83 % yield). ^{1}H NMR (400 MHz, CDCl$_3$, δ, ppm): 8.13 (d, $^3J_{H-H}$ = 4.8 Hz, H6 and H4 pym, 2H), 7.51–7.33 (m, Ph, 10H), 6.65 (d, $^2J_{H-P}$ = 8.9 Hz, NH, 1H), 6.57 (t, $^3J_{H-H}$ = 4.8 Hz, H5 pym, 1H). ^{31}P{^{1}H} NMR (162.0 MHz, CDCl$_3$, δ, ppm): δ 19.76. IR (KBr, ν, cm^{-1}): 3126, 1598 (NH), 3052 (C–H), 1303 (C=C–N), 918 (P–N). Anal. Calc. (%) for C$_{16}$H$_{14}$N$_3$P, C, 68.81; H, 5.05; N, 15.05. Found (%), C, 68.61; H, 4.99; N, 14.97. M$_P$: 123 °C.

2.2.2 N,2-Bis(diphenylphosphino)benzeneamine (Ph$_2$PNHC$_6$H$_4$PPh$_2$)

This ligand was previously reported by Woollins et al. [27]. We describe here a more convenient procedure that does not involve the use of organolithium reagents. A mixture of Ph$_2$Pan (1.0 g, 3.6 mmol) and triethylamine (1.8 mL, 12.5 mmol) was dissolved in THF (20 mL). The solution was cooled at 0 °C and Ph$_2$PCl (0.6 mL, 3.6 mmol) was slowly added. The reaction was allowed to reach room temperature and stirred further for 2 h. After this time, the ammonium salt was separated by filtration and the solvent was removed under vacuum. The oily residue obtained was dissolved in CHCl$_3$ and precipitated with Et$_2$O, producing a white powder (yield, 65 %). ^{1}H NMR (400 MHz, CDCl$_3$, δ, ppm): δ 7.22–7.12 (m, 21 H), 6.76 (dd, $^3J_{H-H}$ = 6.6, 5.9 Hz, 1H), 6.64 (dd, $^3J_{H-H}$ = 7.2, 7.3 Hz, 1H), 5.35 (dd, $^3J_{H-H}$ = 8.4, 8.4 Hz, 1H), 4.02 (s, NH). ^{31}P{^{1}H} NMR (162.0 MHz, CDCl$_3$, δ, ppm): 24.14 (J$_{P-P}$ = 3.5 Hz), −22.68 (J$_{P-P}$ = 3.5 Hz). Anal. Calc. (%) for C$_{30}$H$_{25}$NP$_2$, C, 78.08; H, 5.46; N, 3.04. Found (%), C, 77.89; H, 5.21; N, 3.14.

2.3 Synthesis of Complexes

2.3.1 [PdCl$_2$(Ph$_2$PNHpym)]

A mixture of PdCl$_2$ (200 mg, 1.12 mmol) and PPh$_2$NHpym (258 mg, 1.12 mmol) was dissolved in CH$_3$CN (30 mL) and heated to reflux for 3 h, producing a yellow precipitate. The suspension was cooled, and the solid was filtered off, rinsed with CH$_3$CN and Et$_2$O and dried under vacuum (yield, 70 %). The solid was recrystallized in CH$_2$Cl$_2$/Et$_2$O. ^{1}H NMR (400 MHz, CDCl$_3$, δ, ppm): 10.82 (br, NH), 9.25 (br, 1H), 8.69 (m, 1H), 7.95–7.61 (m, Ph, 10H), 7.14 (m, 1H). ^{31}P{^{1}H} NMR (162.0 MHz, CDCl$_3$, δ, ppm): 65.06. IR (KBr, ν, cm^{-1}): 3084, 1564 (NH); 3064 (C=C–H); 1432 (C=C–N); 923 (P–N). Anal. Calc. (%) for PdCl$_2$C$_{16}$H$_{14}$N$_3$P: C, 42.09; H, 3.09; N, 9.20. Found (%), C, 42.81; H, 3.51; N, 9.22. M$_p$(°C): 202 (with decomposition).

2.3.2 [PdCl$_2$(Ph$_2$Pan)]

In this paper we describe an improved procedure of the synthesis of this complex which have been previously described [28]. A mixture of PdCl$_2$ (200 mg, 1.13 mmol) and Ph$_2$Pan (313 mg, 1.13 mmol) was dissolved in CH$_3$CN (20 mL) and heated to reflux for 3 h producing a green precipitate. The suspension was cooled, and the solid was filtered off, rinsed with CH$_3$CN and Et$_2$O and dried under vacuum. The solid was recrystallized in CH$_2$Cl$_2$/Et$_2$O (65 % yield). ^{1}H NMR (400 MHz, CDCl$_3$, δ, ppm): 7.86 (s, NH$_2$), 7.78–7.54 (m, Ph, 12H), 7.48 (dd, $^3J_{H-H}$ = 7.8 and 3.0 Hz, 1H), 7.42 (pseudo t, $^3J_{H-H}$ = 7.2 Hz, 1H). ^{31}P{^{1}H} NMR (162.0 MHz, CDCl$_3$, δ, ppm): 45.27. Anal. Calc. (%) for PdCl$_2$C$_{18}$H$_{16}$NP: C, 47.55; H, 3.55; N, 3.08. Found (%), C, 48.05; H, 3.65; N, 3.18. M$_p$(°C): 198 (with decomposition).

2.3.3 [Pd(Ph$_2$Pan)$_2$]Cl$_2$

A mixture of PdCl$_2$ (200 mg, 1.13 mmol) and PPh$_2$Pan ligand (626 mg, 2.30 mmol) was dissolved in toluene (20 mL) and heated to reflux for 7 h producing a yellow solution. Half of the solvent was evaporated under vacuum and Et$_2$O was added to precipitate a yellow solid that was recrystallized in CHCl$_3$/Et$_2$O (75 % yield). ^{1}H NMR (400 MHz, CDCl$_3$, δ, ppm): δ 8.86 (s, NH), 7.68–7.50 (m, 12H), 7.46 (pseudo t, $^3J_{H-H}$ = 7.76 Hz, 1H), 7.42 (pseudo t, $^3J_{H-H}$ = 7.64 Hz, 1H). ^{31}P{^{1}H} NMR (162.0 MHz, CDCl$_3$, δ, ppm): 44.32. Anal. Calc. (%) for C$_{36}$H$_{32}$Cl$_2$N$_2$P$_2$Pd: C, 59.08; H, 4.41; N, 3.83. Found (%): C, 58.45; H, 4.65; N, 3.68. M$_p$(°C): 209.

2.3.4 [PdCl₂(Ph₂PNHC₆H₄PPh₂)]

In this work we describe a more direct procedure of the synthesis of this complex which have been previously described [29].

A mixture of PdCl₂ (200 mg, 1.13 mmol) and PPh₂-NHC₆H₄PPh₂ (352 mg, 1.13 mmol) was dissolved in CH₃CN (20 mL) and heated to reflux for 3 h, producing a yellow precipitate. The suspension was cooled, and the solid was filtered off, rinsed with CH₃CN and Et₂O, and dried under vacuum. The solid was recrystallized in CHCl₃/Et₂O (87 % yield). ^{1}H NMR (400 MHz, CDCl₃, δ, ppm): 8.46 (t, $^3J_{H-H}$ = 6.1 Hz, 1H), 7.70–7.46 (m, Ph, 20H), 7.42 (t, $^3J_{H-H}$ = 7.6 Hz, 1H), 7.14 (dd, $^3J_{H-H}$ = 7.2, 6.5 Hz, 1H), 6.93 (t, $^3J_{H-H}$ = 7.5 Hz, 1H), 6.55 (m, 1H). ^{31}P{^{1}H} NMR (162.0 MHz, CDCl₃, δ, ppm): 80.48 (d, J_{P-P} = 12 Hz, *P*–N), 17.3 (d, J_{P-P} = 12 Hz, *P*–C). Anal. Calc. (%) for PdCl₂C₃₀H₂₅NP₂: C, 56.41; H, 3.94; N, 2.19. Found (%): C, 56.77; H, 4.09; N, 2.18. Mₚ(°C): 187° (with decomposition).

2.4 Complex Reactivity

The study was carried out through the analysis of the ^{31}P{^{1}H} NMR spectra of solutions obtained by mixing complexes [PdCl₂(*P,X*)] (*P,X* = Ph₂PNHpym, Ph₂Pan and Ph₂PNHC₆H₄PPh₂) and the free ligands or PPh₃ at different molar ratio. Toluene-d_8, acetonitrile-d_3 or CDCl₃ were used as solvents. NMR spectra were registered in a Bruker 300 MHz spectrometer under inert atmosphere, 10 min after the reagents were mixed.

2.5 Single-Crystal X-ray Diffraction

Crystals of [Pd(Ph₂Pan)₂]Cl₂·(Ph₂Pan)₂ were grown by slow diffusion of Et₂O to a solution prepared by dissolving [PdCl₂(Ph₂PPan)] and an excess of ligand in CHCl₃. The crystal structure was determined at 293 K on a needle-shaped single crystal with dimensions of 0.29 mm × 0.26 mm × 0.14 mm. Data collection was carried out on a SMART CCD diffractometer, using the ω-scans technique. Data reduction was performed with SAINT (SAINTPLUS V6.22; Bruker AXS), while the structure was solved by direct methods. Completion and refinement was conducted with SHELXL package (SHELXTL NT/2000, Version 6.10; Bruke AXS). Empirical absorption corrections were applied using SADABS V2.05: Bruker AXS.

Crystal data for [Pd(Ph₂Pan)₂]Cl₂·(Ph₂Pan)₂: C₇₂H₆₄Cl₂N₄P₄Pd, M = 1286.45, monoclinic, space group C2/c, a = 10.108(2) Å, b = 19.040(4) Å, c = 32.887(7) Å, β = 92.31(3)°, V = 6324(2) Å³, Z = 4, R₁ = 0.0554, wR₂ = 0.0974 (all data), R₁ = 0.0402, wR₂ = 0.0914 (for all observed data I ≥ 2σ(I)), Goodness-of-fit on F² = 0.985 for 571 parameters and 12,046 independent reflections, largest residuals in F map 0.485 and −0.207 e Å⁻³.

2.6 Catalytic Methoxycarbonylation

The catalytic reactions were carried out in a glass-lined stainless steel autoclave equipped with a temperature control unit and a sampling valve. In a typical experiment, the palladium complex (7.7 mg, 4.0 × 10⁻² mmol), TsOH (69 mg, 4.0 × 10⁻¹ mmol) and 2.5 g of styrene (24.0 mmol) were dissolved in a mixture of toluene (15 mL) and methanol (5 mL). The solution was introduced into the reactor and three cycles of vacuum/CO were applied to finally charge the autoclave with 50 bar of CO at 75 °C. Samples of the reaction mixture were periodically extracted to be analyzed by GC and the pressure was adjusted if necessary.

3 Results and Discussion

Complexes [PdCl₂(*P,X*)] (where *P,X* = Ph₂PNHpym, Ph₂Pan or PPh₂NHC₆H₄PPh₂), were obtained in moderate to good yields in acetonitrile, by reaction of PdCl₂ and the ligand in equimolar ratio (see Scheme 2). Furthermore, the reaction of complexes [PdCl₂(*P,X*)] (where *P,X* = Ph₂PNHpym, Ph₂Pan) with a further equivalent of ligand yield the ionic complexes [Pd(*P,X*)₂]Cl₂ (δ(P) = 44.3 ppm for [Pd(Ph₂Pan)₂]Cl₂ and δ(P) = 85.1 ppm for [Pd(Ph₂PNHpym)₂]Cl₂.

The ^{31}P NMR study also revealed that the neutral complexes [PdCl₂(*P,X*)] (X=N) react with 1 equivalent of PPh₃ to form the ionic complexes [PdCl(PPh₃)(*P,X*)]Cl (*P,X* = Ph₂Pan, Ph₂PNHpym). In these complexes, the PPh₃ is disposed *trans* to the nitrogen donor atom, as revealed by the small J_{P-P} coupling constant (J_{P-P} = 7 Hz, δ(P) = 45.1 and 35.4 ppm for *P,X* = Ph₂Pan and J_{P-}
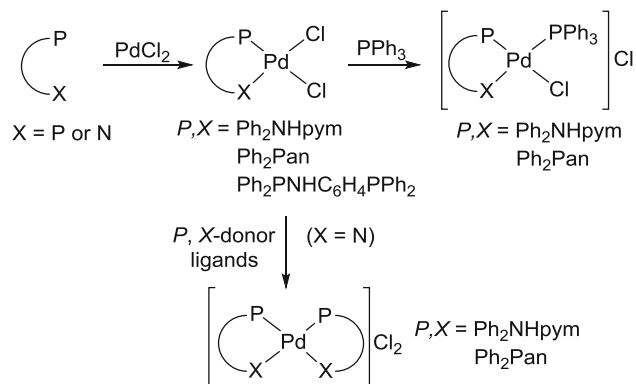

Scheme 2 Reactions of the PdCl₂ compound with the phosphorus–nitrogen ligand

$_P = 9$ Hz, $\delta = 81.3$ and 37.5 ppm for $P,X = PPh_2$-NHpym), characteristic of two phosphorus atoms coordinated in *cis* positions. Contrary to the complexes of the *P,N*-donor ligands, the species [PdCl$_2$(PPh$_2$NHC$_6$H$_4$PPh$_2$)] does not react neither with PPh$_3$ nor with an additional equivalent of ligand. In summary, while the neutral complexes of the heterobidentate ligands readily exchange a chloro by a phosphine ligand, in the case of the bidentate *P*-donor ligand, the neutral complex seems to be more inert.

In order to unequivocally establish the stereochemistry of the [Pd(Ph$_2$Pan)$_2$]Cl$_2$ complex, crystals of the compound were grown in chloroform/Et$_2$O in a solution containing an excess of the ligand, with enough quality for X-ray diffraction. Analysis of the X-ray data shows that the complex salt crystallizes with two molecules of free ligand, [Pd(Ph$_2$Pan)$_2$]Cl$_2$·(Ph$_2$Pan)$_2$. The crystal structure shows an extensive H-bonding network between the chloride anions and the amine moiety of the ligands, both the coordinated and the non-coordinated ones. In particular, each of the two chloride anions is involved in three H-bonds, two of them with hydrogen of each one of the N atoms of the complex (N–Cl distances ranging from 3.03 to 3.27 Å), and a third weaker H-bond (N–Cl distances 3.40 and 3.50 Å) with one of the free ligands. In other words, as expected for their higher acidity, both protons of the NH$_2$ of the metal-coordinated amines are involved in H-bonding, but only one proton is involved from the NH$_2$ of each free ligand.

A structure of the [Pd(Ph$_2$Pan)$_2$]$^{2+}$ cation with the most relevant distances and angles is shown in Fig. 2.

The Pd atom shows a *cis* square-planar environment. In this micro symmetry the following angles were observed:
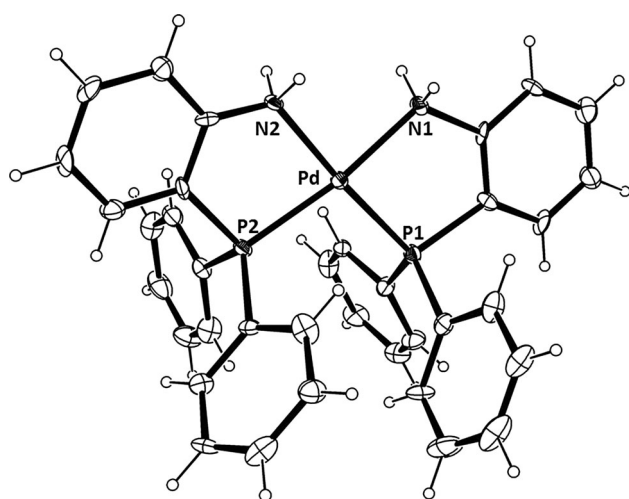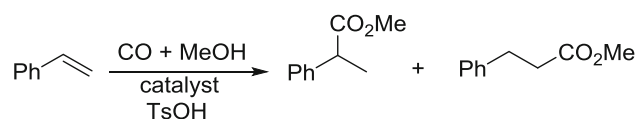
N–Pd–P bite angles of the ligand (85.8° and 82.8°); P1–Pd–P2 angle (101.39°), while the N1–Pd–N2 angle is 90°. The orientation of one phenyl group of each phosphorus suggests that a π–π stacking could be partially responsible for the stabilization of the *cis* arrangement around the metal.

Complexes [PdCl$_2$(PPh$_2$PNHpym)], [PdCl$_2$(PPh$_2$Pan)] and [PdCl$_2$(PPh$_2$PNHC$_6$H$_4$PPh$_2$)] were used as catalysts for the methoxycarbonylation of styrene (Scheme 3). Results are collected in Table 1.

Methoxycarbonylation reactions were carried out in optimized conditions (P, T, solvent) for related catalytic systems [23]. Table 1 shows that complexes [PdCl$_2$(*P,N*)] (*P,N* = PPh$_2$PNHpym or Ph$_2$Pan) are only moderately active (ca. 50 % conversion in 6 h) and chemoselective (ca. 75 %), while they achieve regioselectivities toward the branched ester in the range 75–82 % (entries 1 and 4). For the complex with the *P*-donor bidentate ligand (entry 7), conversion and chemoselectivity are better (70 and 92 % respectively) than with complexes of the heterobidentate ligands, but the regioselectivity is worse (58 %), as expected for a bidentate P-onor ligand. When an additional equivalent of the bidentate ligand is added to each one of the complexes, both the conversion and selectivities improve for the two heterobidentate ligands (entries 2 and 5), but the opposite happens with the *P*-donor bidentate ligand (entry 8). Remarkably, the complex with the pyrimidine ligand [PdCl(Ph$_2$PNHpym)(PPh$_3$)]Cl, generated in situ by reaction between the neutral complex and PPh$_3$, achieves practically complete conversion and chemoselectivity and 97 % regioselectivity in the branched ester (entry 3), as it happens with its pyridine analog [23]. This comparable result with the pyridine ligand indicates that the reported rollover cyclometalation of the aromatic ring in related complexes [24], which is prevented in the pyrimidine ligand, does not have a contribution to the noteworthy performance of the catalysts [PdCl(*P,X*)(PPh$_3$)]Cl *P,X* = Ph$_2$PNHpy and Ph$_2$PNHpym. Likewise in the case of the [PdCl$_2$(Ph$_2$Pan)] complex, the addition of one equivalent of PPh$_3$, to generate in situ the cationic complex [PdCl(Ph$_2$Pan)(PPh$_3$)]Cl, leads to an active and selective catalyst (entry 6), but its performance is not as good as with [PdCl(Ph$_2$PNHpym)(PPh$_3$)]Cl. As expected for the inertness of [PdCl$_2$(Ph$_2$PNHC$_6$H$_4$PPh$_2$)], the addition of PPh$_3$ to this complex does not significantly modify its catalytic performance. Finally, catalysts obtained in situ

Fig. 2 Molecular structure of the [Pd(Ph$_2$Pan)$_2$]$^{2+}$ complex cation. Relevant distances (Å) and angles (°): P1–Pd, 2.242(3); P2–Pd, 2.257(2); N1–Pd, 2.114(7); N2–Pd, 2.079(7); P1–Pd–N1, 85.8(2); P2–Pd–N2, 82.8(2); N1–Pd–N2, 89.99(10); P1–Pd–P2, 101.39(3)

Scheme 3 Methoxycarbonylation reaction of styrene

Table 1 Methoxycarbonylation styrene with palladium complexes

| Entry	Complex	L added (1 equiv.)	Con.[a] (%)	Chem.[b] (%)	Reg.[c] (%)
1	[PdCl$_2$(Ph$_2$PNHpym)]	–	48	71	75
2	[PdCl$_2$(Ph$_2$PNHpym)]	Ph$_2$PNHpym	78	81	92
3	[PdCl$_2$(Ph$_2$PNHpym)]	PPh$_3$	99	99	97
4	[PdCl$_2$(Ph$_2$Pan)]	–	46	75	82
5	[PdCl$_2$(Ph$_2$Pan)]	Ph$_2$Pan	76	85	96
6	[PdCl$_2$(Ph$_2$Pan)]	PPh$_3$	92	93	96
7	[PdCl$_2$(Ph$_2$PNHC$_6$H$_4$PPh$_2$)]	–	70	92	58
8	[PdCl$_2$(Ph$_2$PNHC$_6$H$_4$PPh$_2$)]	Ph$_2$PNHC$_6$H$_4$PPh$_2$	62	88	46
9	[PdCl$_2$(Ph$_2$PNHC$_6$H$_4$PPh$_2$)]	PPh$_3$	77	91	66
10	[Pd(PPh$_3$)$_4$]	Ph$_2$PNHpym	55	91	65
11	[Pd(PPh$_3$)$_4$]	Ph$_2$Pan	67	92	63
12	[Pd(PPh$_3$)$_4$]	Ph$_2$PNHC$_6$H$_4$PPh$_2$	65	90	63

Reaction conditions: 4.0×10^{-2} mmol of Pd complex; substrate/TsOH/catalyst = 600/10/1; solvent: toluene 15 mL + methanol 5 mL; T = 75 °C; P(CO) = 50 bar; t = 6 h

[a] % of styrene converted

[b] % of esters formed from the converted styrene

[c] % of branched ester from the total esters formed

Scheme 4 Alternative paths for methoxycarbonylation of styrene
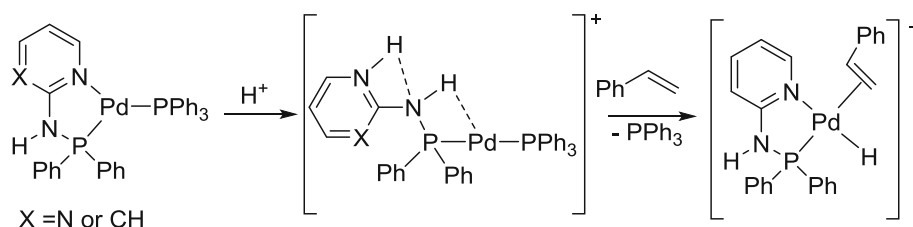
by reacting equimolar amounts of [Pd(PPh$_3$)$_4$] and the three ligands were essayed (entries 10–12), showing very similar and moderate performances. Interestingly, not only the conversion achieved by the in situ formed catalyst [Pd(PPh$_3$)$_4$] + Ph$_2$PNHpym is significantly lower than the one obtained with the cationic system [PdCl(Ph$_2$-PNHpym)(PPh$_3$)]Cl, but also the selectivity in the branched ester is worse with the Pd(0) precursor than with the Pd(II) complex. A similar difference was observed between the Pd(II) ad Pd(0) catalysts for the Ph$_2$Pan ligand. However, very similar results both in activity and selectivity were achieved with the Pd(II) complex and with Pd(0) in situ formed catalyst in the case of the *P*-donor bidentate ligand Ph$_2$PNHC$_6$H$_4$PPh$_2$. These results indicate that in the case of *P,N*-heterobidentate ligands the catalytic species formed from [Pd(PPh$_3$)$_4$] plus the ligand are different than those produced from the cationic complex, while in case of the *P*-donor bidentate ligand both catalytic pecursors likely evolve to same catalytic active species.

In summary, these catalytic experiments confirm that [PdCl(Ph$_2$PNHpy)(PPh$_3$)]Cl and its pyrimidine analog here described are particularly appropriate catalysts for an efficient and selective methoxycarbonylation of styrene.

A DFT study of the mechanism of the propyne methoxycarbonylation to produce methyl methacrylate, catalyzed by a Pd complex of 2-pyridyldiphenylphosphine ligand and methanesulphonic acid (MesOH) co-catalyst, has been recently reported [13]. This study proposes two steps where the hemilabile ability of the *P,N*-donor ligand plays a crucial and distinctive role. In the first step, an intramolecular hydrogen transfer from a pyridinium fragment, arising from the protonation of the pyridine moiety by the acid co-catalyst, to the coordinated alkyne takes place. The second step is the methanolysis of the acyl fragment. For this step, a hydrogen bond between pyridine and methanol facilitates the nucleophilic attack of the alcohol. The similarities among this process and the methoxycarbonylation of styrene here described, both catalyzed by a palladium complex with *P,N*-ligand, seem evident. It is possible that the methanolysis step in both cases follows parallel paths. However, the first step, leading to the alkyl intermediate in the case of styrene or the

vinyl intermediate for the propyne, must differ. While protonation of a coordinated alkyne is a well-known process, the direct protonation of the coordinated styrene is unlikely. As an alternative path (Scheme 4), we propose that the tricoordinated Pd(0) complex [Pd(Ph$_2$-PNHpym)(PPh$_3$)] undergoes protonation of a pyrimidine (or pyridine) nitrogen, followed by an intramolecular oxidative addition of the NH from the Ph$_2$P-NH fragment to the metal, concerted with a proton transfer from the pirimidinium moiety to the Ph$_2$P-N$^-$ fragment, followed by the coordination of the pyrimidine moiety to the Pd(II) center. Styrene would then coordinate to the Pd-hydrido species to undertake a classical migration of the hydride to form the Pd(II)-alkyl complex intermediate.

4 Conclusions

Complexes [PdCl(PPh$_2$PNHpy)(PPh$_3$)]Cl and [PdCl(PPh$_2$-PNHpym)(PPh$_3$)]Cl containing 2-(diphenylphosphinoamino)pyridine (Ph$_2$PNHpy) and 2-(diphenylphosphinoamino)pyrimidine (Ph$_2$PNHpym) are remarkably active and chemo- and regioselectives in the methoxycarbonylation of styrene in presence of p-toluene sulfonic acid, whose concentration was minimized in this study. Their outstanding performance seems to be related with both the presence of a potentially hemilabile imine coordination (pyridine or pyrimidine), as well as with the presence of the NH fragment of the amidophosphine fragment, although the structurally related complex with the 2-(diphenylphosphino)aniline ligand performs only slightly worse than heterocyclic ligands. The nearly identical result achieved with catalysts containing pyridine and pyrimidine fragments precludes any involvement of a rollover cyclometalation step in the catalytic process. Finally, when the N-donor atom is replaced by a phosphine both the conversion and the selectivity dramatically drop.

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